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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,484	08/03/2006	David Gutig	82498	1037

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,484	GUTIG, DAVID	
	Examiner	Art Unit	
	TERESA E. STRZELECKA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *17-20 and 23-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,21 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 1-23, species G) in the reply filed on February 20, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 17-20 and 23-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on February 20, 2009.

3. Claims 1-16, 21 and 22 will be examined.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on January 5, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Interpretation

5. Applicant did not define the term "activation-induced cytidine deaminase-AID", therefore any cytidine deaminase is considered to anticipate this term.

6. Applicant did not define the term "amplification", therefore it is interpreted as any extension reaction catalyzed by a polymerase.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of cytidine deaminases which have not been described. The genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named cytidine deaminase, called AID by Applicant, and characterized by citations from different references (see pages 4 and 5). However, no specific sequence encoding the AID protein or its amino acid sequence were provided. Further, no fragments or modifications which can perform the function of deaminating cytidine were provided. No structural limitations or requirements which provide guidance on the identification of polypeptides which meet these functional limitations are provided.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the term "acitivation-induced cytidine deaminase" lacks any specific structure and is precisely the situation of naming a type of material which is generally known to likely exist, but, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "acitivation-induced cytidine deaminase or a biologically active fragment of AID or a modification thereof", for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a deaminase, without any definition of the particular polypeptides claimed.

In the application at the time of filing, there is no record or description which would demonstrate conception of any specific AID. Therefore, the claims fail to meet the written description requirement by encompassing proteins which are not described in the specification.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-16, 20 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are written in the passive tense. Method claims should recite positive, active process steps (see Ex parte Erlich 3 USPQ 2d 1011). This rejection may be overcome by amending the claims to recite the active tense, e.g. "bringing the DNA into contact with cytidine deaminase," etc.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 1-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Bransteitter et al. (PNAS USA, vol. 100, pp. 4102-4107, April 2003; cited in the IDS).

Regarding claim 1, Bransteitter et al. teach a method for the detection of cytosine methylations in DNA (Abstract) characterized in that

a) the DNA to be investigated is brought into contact with a cytidine deaminase, whereby the cytidine deaminase deaminates cytidine and 5-methylcytidine at different rates (page 4102, paragraphs 3-5),

b) the partially deaminated DNA is investigated with respect to its sequence (page 4102, last paragraph; page 4103, first and second paragraph), and

c) from the presence or the proportion of deaminated positions, conclusions can be made on the methylation status of the DNA to be investigated in said positions (Fig. 1; Fig. 2).

Regarding claim 2, Bransteitter et al. teach AID (page 4102, fourth paragraph).

Regarding claims 3 and 4, Bransteitter et al. teach single-stranded and partially-single stranded DNA (page 4102, third paragraph; Table 1).

Regarding claims 5-7, Bransteitter et al. teach single stranded regions being between 3 and 20 nucleotides long, between 5 and 12 nucleotides long and 9 nucleotides long (Table 1, page 4106).

Regarding claims 8 and 9, Bransteitter et al. teach oligomers between the length of 20 to 150 nucleotides and 35-60 nucleotides (Table 1, page 4106).

Regarding claims 10 and 11, Bransteitter et al. teach oligomers concentration of 100 nM (page 4102, fifth paragraph), anticipating the claimed ranges.

Regarding claims 12 and 13, Bransteitter et al. teach amplification of the deaminated fragment using a polymerase (page 4103, second paragraph).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 12-16, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bransteitter et al. (PNAS USA, vol. 100, pp. 4102-4107, April 2003; cited in the IDS) and Olek et al. (U.S. Patent No. 7,229,759 B2).

A) Bransteitter et al. teach detection of the converted uracil residues using primer extension and ddA, but do not teach PCR or real-time PCR or using blocker oligonucleotides in the amplification reaction.

B) Regarding claims 12-14, 21 and 22, Olek et al. teach detection of deaminated cytosines resulting from bisulfite reaction using real-time PCR (col. 5, lines 37-53; col. 13, lines 45-59).

Regarding claim 15, Olek et al. teach methylation-specific primers (col. 2, lines 56-67; col. 3, lines 1, 2; col. 11, lines 15-31).

Regarding claim 16, Olek et al. teach using blocking oligonucleotides during amplification (col. 6, lines 3-20 and 38-67; col. 11, lines 29-49).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the amplification methods of Olek et al. with blocking oligonucleotides to detect the converted cytidines in the method of Bransteitter et al. The motivation to do so is provided by Olek et al. (col. 13, lines 52-59 and col. 11, lines 67 and col. 12, lines 1-3):

"A particularly preferred variant of the method, however, is the simultaneous detection of qualifier positions and classifier positions in one experiment, which can be achieved by the use of TaqMan or LightCycler technology variants. Additional fluorescently labeled oligonucleotides are to be added to the oligonucleotides, which provide for a preferred amplification of the DNA to be investigated, and the change in fluorescence is measured during the PCR reaction. In principle, since the DNA to be investigated is amplified, information on the methylation status of different classifier CpG positions is obtained predominantly also directly from this change in fluorescence. Since different oligonucleotides are each preferably provided with different fluorescent dyes, a distinction of the change in fluorescence during the PCR is also possible, separately for different positions."

"If only one small group of CpGs is available and still a high amount of background DNA has to be blocked, it is therefore preferred that one part of this group of CpGs is covered by a methylation specific primer and the other part is covered by a methylation specific blocking probe,

and the binding site of this non-extendible probe could ideally even overlap with the binding site of the primer. This way, high relative sensitivity, this means highly preferred amplification of the DNA to be analyzed while suppressing the background DNA, can be achieved with only a small group of CpGs as Qualifier positions."

15. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner
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Primary Examiner, Art Unit 1637
June 2, 2009